Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Late Breaking

TOPIC: Critical Care

TYPE: Late Breaking

C-REACTIVE PROTEIN AS A BIOMARKER FOR IMPROVED EFFICACY OF LENZILUMAB IN PATIENTS WITH COVID-19: RESULTS FROM THE LIVE-AIR TRIAL

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PURPOSE: The hyperinflammatory cytokine storm (CS) of COVID-19 is mediated by GM-CSF leading to release of downstream inflammatory chemokines, cytokines, and corresponding markers of systemic inflammation (C-reactive protein, CRP). The LIVE-AIR study demonstrated that treatment with lenzilumab, an anti-GM-CSF monoclonal antibody in patients hospitalized with COVID-19, safely improved the likelihood of achieving the primary endpoint, survival without ventilation (SWOV) by 1.54-fold (HR: 1.54; 95%CI: 1.02-2.32, p=0.0403) compared with placebo. An exploratory analysis in patients with CRP <150 mg/L and aged <85 years was conducted to determine the effect of lenzilumab when administered prior to advanced inflammation.

METHODS: LIVE-AIR was a phase 3 randomized, double-blind, placebo-controlled trial. Patients with COVID-19 (n=520), ≥18 years, and ≤94% oxygen saturation on room air and/or requiring supplemental oxygen, but not invasive mechanical ventilation (IMV), were randomized to receive lenzilumab (600 mg, n=261) or placebo (n=259) via three intravenous infusions administered 8 hours apart. Participants were followed through Day 28 following treatment.

RESULTS: Overall, baseline demographics were comparable between the two treatment groups: male, 64.7%; mean age, 60.5 years; mean BMI, 32.5 kg/m^2; median CRP, 79 mg/L; CRP was <150 mg/L in 78% of participants. Participants received steroids (93.7%), remdesivir (72.4%), or both (69.1%). Lenzilumab (n=159) improved the likelihood of SWOV by 3.04-fold in participants with CRP < 150 mg/L and age < 85 years (3.04; 1.68-5.51, nominal p=0.0003) compared with placebo (n=178). Response to lenzilumab was observed in the first through third quartiles of baseline CRP (<41 mg/L, HR:8.33; 41-<79 mg/L, HR:1.60; 79-<137 mg/L, HR: 2.12; >137 mg/L, HR: 1.17). The incidence of IMV, ECMO, or death was reduced (OR: 0.31; 95%CI: 0.15-0.63, p=0.002) and mortality was improved by 2.22-fold (OR: 2.22; 95%CI: 1.07-4.67, p=0.034). In these participants, lenzilumab decreased CRP as early as Day 2 following treatment, compared with placebo which was further decreased by 38% on Day 28 compared with placebo (24.4±3.4 mg/L vs 39.1±4.9 mg/L).

CONCLUSIONS: Lenzilumab significantly improved SWOV in hospitalized, hypoxic participants with COVID-19 pneumonia with the greatest benefits in SWOV and survival in patients with CRP<150 mg/L and age <85 years. Inhibition of GM-CSF, an orchestrator of CS, early in the hyperinflammatory response improved outcomes in COVID-19. NCT04351152

CLINICAL IMPLICATIONS: CRP, a routine laboratory test can be used to determine in which patients, and at what times, lenzilumab treatment may provide the greatest clinical benefits and outcomes.

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